

PATENT COOPERATION TREATY

22 MAY 2002

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 66040-9675	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/13687	International filing date (day/month/year) 18 MAY 2000	Priority date (day/month/year) 21 MAY 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant BOARD OF CONTROL OF MICHIGAN TECHNOLOGICAL UNIVERSITY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and or drawings which have been amended and are the basis for this report and or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

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OCT 07 2002

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Date of submission of the demand 21 DECEMBER 2000	Date of completion of this report 04 APRIL 2002
Name and mailing address of the IPEA, US Commissioner of Patents and Trademarks Box 187 Washington, D.C. 20331 Facsimile No. 703 305-8230	Authorized officer <i>Medina A Ibrahim</i> MEDINA A IBRAHIM Telephone No. 703 308-0196

I. Basis of the report1. With regard to the **elements** of the international application: *☒ the international application as originally filed☒ the description:pages 1-34 as originally filedpages NONE filed with the demandpages NONE filed with the letter of _____☒ the claims:pages 35-39 as originally filedpages NONE as amended (together with any statement) under Article 19pages NONE filed with the demandpages NONE filed with the letter of _____☒ the drawings:pages 1-10 as originally filedpages NONE filed with the demandpages NONE filed with the letter of _____☒ the sequence listing part of the description:pages 1-15 as originally filedpages NONE filed with the demandpages NONE filed with the letter of _____2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:☒ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets fig. NONE5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)) **

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15687

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

Please See Supplemental Sheet.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. 1-4.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/13657

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. citations and explanations (Rule 70.7)

Claims 1-4, 9-16, 26-31, 35, 40, 42-43, and 45-46 lack novelty under PCT Article 33(2) as being anticipated by CALGENE, INC. (WO 98/18949). This objection is repeated for the same reasons as set forth in the Written Opinion.

Applicants' response filed on 29 November 2001, have been fully considered. Applicants' argument regarding the biological, physiological and utility difference as well as the quality of cellulose between aspen tree and cotton are not found persuasive because all these limitations are not recited in the objected claims. The claims recite a polynucleotide having SEQ ID NO.1 or 4, or a fragment thereof encoding a functional domain of cellulose synthase, and a method of altering the growth of a plant by expressing said sequences.

CALGENE, INC. teaches a vector comprising an isolated DNA sequence encoding a plant cellulose synthase, and a method of using said vector to modify the woody quality a plant by expressing said DNA in sense or antisense orientation with respect to a promoter, and transgenic cotton plants with modified cellulose content.

While CALGENE does not teach Applicant's SEQ ID NO.1-2 and 4-5, the claimed fragment which only needs to encode a functional domain of a cellulose synthase is anticipated by the reference, based on the definition of a "fragment" in Applicant's description, page 7, lines 27-31. The cellulose synthase gene from cotton encodes a functional domain of a cellulose synthase gene, therefore, would inherently comprise the claimed fragment encoding a functional domain of a cellulose synthase. CALGENE, INC. also teaches a method for altering the woody quality of a plant using a cellulose synthase gene operably linked in sense or antisense orientation to a promoter. Therefore, the claims lack novelty under PCT Article 33(2).

Claims 5-7 lack novelty under PCT Article 33(2) as being anticipated by Walter et al (US 5, 633, 439), for the same reasons as set forth in the Written Opinion of 29 October 2001.

Applicants' arguments in page 4 of the response have been (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15627

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/05, 15/09, 15/29, 15/52, 15/82; A01H 5/00 and US Cl.: 800/278, 286, 287, 295, 298; 435/69.1, 320.1, 419; 536/23.2, 23.6, 24.1, 24.5

IV. LACK OF UNITY OF INVENTION:

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2, and 13.3 is not complied with for the following reasons:

As applicant was previously notified this International Preliminary Examining Authority has found plural inventions claimed in the International Application covered by the claims indicated below:

Applicants' payments for extra groups both in the Search Report and in the Written Opinion are acknowledged.

Group I, claim(s) 1-4, 9-31, 35, 40, 42-43, 45-46, drawn to polynucleotide having specific nucleic acid sequence or a fragment thereof encoding a functional domain of a cellulose synthase, methods of altering cellulose content of a transgenic plant.

Group II, claim(s) 5-7, 32, 36-39, 41, and 44, drawn to cellulose synthase promoters and methods of their use.

Group III, claim(s) 8 and 18, drawn to cellulose synthase polypeptides

Group IV, claim(s) 33-34, drawn to a method of identifying regulatory elements in a cellulose synthase promoter.

Applicant's argument against the lack of unity of the inventions listed as Groups I-IV have been fully considered but was not found persuasive.

Applicant's argue that the claims are but different aspects of the same disclosed subject matter, as they all relate to cellulose synthase expression, which would be covered in a single search.

In response to Applicant's argument, the "expression of a cellulose synthase" in a plant does not constitute a single special technical feature which would be an advance over the prior art, as evidenced by the art rejections. In addition, Applicant's assertion that all groups would be covered by a single search is incorrect because the search required by one group is not required by any of the other groups.

For the reasons discussed above and in the Written opinion, inventions I-IV lack unity of invention.

V. 1. REASONED STATEMENTS:

The report as to Novelty was positive (YES) with respect to claims 17, 19-24, 32-34, 36-39, 41 and 44.

The report as to Novelty was negative (NO) with respect to claims 1-16, 18, 25-31, 35, 40, 42-43, and 45-46.

The report as to Inventive Step was positive (YES) with respect to claims 32-34, 36-39, 41, and 44.

The report as to Inventive Step was negative (NO) with respect to claims 1-31, 35, 40, 42-43, and 45-46.

The report as to Industrial Applicability was positive (YES) with respect to claims 1-46.

The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

considered, but are not found persuasive.

the claims recite "a functional fragment" or a "fragment" of a cellulose synthase promoter, and a transgenic plant comprising said fragment. According to the definitions provided in Applicant's description, the claimed fragment need only to have "a promoter activity." Walter et al teach an isolated CAD promoter, in a vector, controlling the expression of a linked gene, and a transgenic plant comprising said promoter. Applicants have provided no specific identifying characteristics which differs the claimed promoter fragment from the prior art promoter. Therefore, the claims lack novelty under PCT Article 33(2).

Claim 8 lacks novelty under PCT Article 33(2) as being anticipated by Ben-Bassat et al (US 5,268, 274), for the same reasons as set forth in the Written Opinion of 29 October 2001.

Applicants' arguments in page 4 of the response have been considered, but are not found persuasive.

The claim is broadly drawn to a polypeptide of SEQ ID NO:2 or 5, or any amino acid sequence with a functional domain of cellulose synthase. While Ben-Bassat does not disclose Applicants' SEQ ID NO: 2 or 5, the claimed "an amino acid sequence

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 11

with a functional domain of cellulose synthase" reads on any cellulose synthase from any source. Therefore, the claim lacks novelty under PCT Article 33(2).

Claim 18 lacks novelty under PCT Article 33(2) as being anticipated by PEAR et al (Proc. Natl. Acad. USA, Vol. 93 pp. 12637-12642, 1996) for the same reasons as set forth in the Written Opinion of 29 October 2001.

Applicants' arguments in page 5 of the response have been considered, but are not found persuasive.

The claim is broadly drawn to a polypeptide comprising a UDP-glucose catalytic subunit of a cellulose synthase which reads on reads on any cellulose synthase from any source with UDP-glucose catalytic subunit. The claim does not recite any distinct feature that differs the claimed polypeptide from that of the prior art. Therefore, the claim lacks novelty under PCT Article 33(2).

Claims 17, and 19-31 lack inventive step under PCT Article 33(3) as being obvious over Secor et al. (Plant Molecular Biology, Vol. 15, pp. 673-683, 1990) in view of Saxena et al. (US 5, 646, 023) for the same reasons as set forth in the Written Opinion of 29 October 2001.

Applicants' arguments in page 6 of the response have been considered, but are not found persuasive.

When considering lack of inventive step, a reference need not teach each and every claim limitations. Obviousness can be established where there is some teachings, suggestions in the prior art reference or from the general knowledge available to one of ordinary skill in the art, with a reasonable expectation of success. Secor et al was relied upon because it provides the reasonable expectation of success to transform a plant with any heterologous gene (whether it is a sucrose biosynthesis gene or not). Saxena et al was relied upon because it teaches a gene for the catalytic subunit of a cellulose synthase, its importance in the biosynthesis of a plant cell wall, and suggests isolation of cellulose synthase gene from higher plants. There is no reason to believe that the transformation of a plant with a cellulose synthase gene, like the one taught by Secor, or the one obtainable from higher plants as suggested by Secor, would be detrimental in the plant. To the contrary, one skilled in the art can successfully transform a plant with a cellulose synthase gene by using the method taught by Secor et al., with a reasonable expectation of success, therefore, the claims lacks inventive step under PCT Article 33(3).

Claims 1-4, 9-16, 25-31, 35, 40, 42-43, and 45-46 lack inventive step under PCT Article 33(3) as being obvious over AUSTRALIAN NATIONAL UNIVERSITY (WO 98/00549), for the same reasons as set forth in the Written Opinion of 29 October 2001.

Applicants' arguments in page 7 of the response have been considered, but are not found persuasive because of the following reasons: Firstly, when considering lack of inventive step, a reference need not to teach each and every claim limitations. Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teachings, suggestion, or motivation to do so found either in the references themselves, or in the knowledge generally available to one of ordinary skill in the art. Secondly, the limitations of biological, physiological, utility-wise distinction, or the transformation protocols between Arabidopsis and Aspen tree are not recited in the rejected claims. Thirdly, while the AUSTRALIAN NATIONAL UNIVERSITY (WO 98/00549) does not disclose Applicants' SEQ ID NO: 1 or 4 encoding SEQ ID NO: 2 or 5, the claims are not limited to these specified sequences but are broadly drawn to cellulose synthase genes from non-aspen source as well as fragments encoding a functional domain of a cellulose synthase. Therefore, In view of the prior art (AUSTRALIAN NATIONAL UNIVERSITY (WO 98/00549), the claimed invention lack an inventive step under PCT Article 33(3), as stated in the Written opinion.

Claims 32-34, 36-39, 41, and 44 meet the criteria set out in PCT Article 33(2) and 33(3) because the prior art does not teach or fairly suggest determination of a mechanical stress responsive element (MSRE) in a cellulose synthase promoter or a method of its use.

Claims 1-46 meet the criteria set out in PCT Article 33(4) because plants with modified cellulose or lignin content have industrial applicability.

----- NEW CITATIONS -----

PEAR et al. Higher Plants Contain Homologs of the Bacterial celA Genes Encoding The Catalytic Subunit of Cellulose Synthase. PNAS, October 1996, Vol. 93, pages 12637-12642.

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
30 November 2000 (30.11.2000)

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(10) International Publication Number
WO 00/71670 A2

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- (21) International Application Number: PCT/US00/13637
- (22) International Filing Date: 18 May 2000 (18.05.2000)
- (25) Filing Language: English
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- (30) Priority Data:
60/135,280 21 May 1999 (21.05.1999) US
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- (81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:
— Without international search report and to be republished upon receipt of that report.
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR ENHANCING CELLULOSE AND MODIFYING LIGNIN BIOSYNTHESIS IN PLANTS

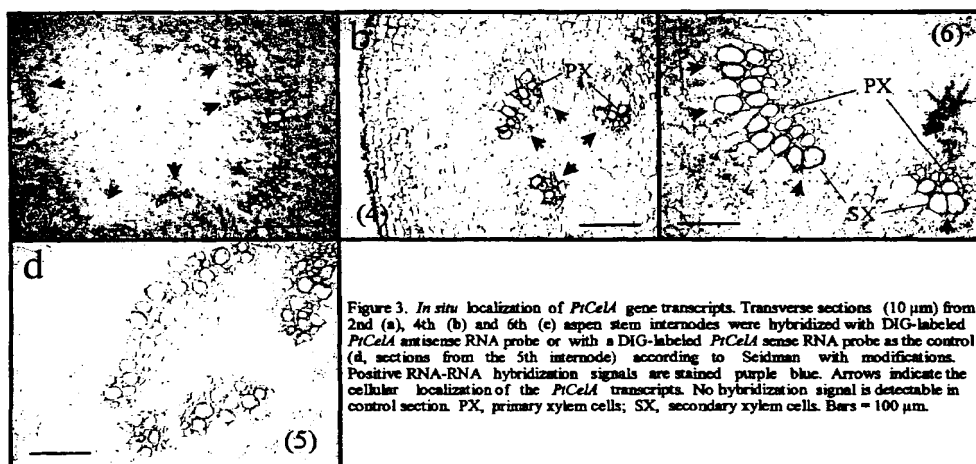


Figure 3. *In situ* localization of *PtCelA* gene transcripts. Transverse sections (10 µm) from 2nd (a), 4th (b) and 6th (c) aspen stem internodes were hybridized with DIG-labeled *PtCelA* antisense RNA probe or with a DIG-labeled *PtCelA* sense RNA probe as the control (d, sections from the 5th internode) according to Seidman with modifications. Positive RNA-RNA hybridization signals are stained purple blue. Arrows indicate the cellular localization of the *PtCelA* transcripts. No hybridization signal is detectable in control section. PX, primary xylem cells; SX, secondary xylem cells. Bars = 100 µm.

(57) Abstract: This invention relates to polynucleotide molecules encoding cellulose synthase, promoters of cellulose synthase and cellulose synthase polypeptides, methods for genetically altering cellulose and lignin biosynthesis, and methods for improving strength properties of juvenile wood and fiber in trees. The invention further relates to methods for identifying regulatory elements in a cellulose synthase promoter and transcription factors that bind to such regulatory elements, and to methods for augmenting expression of polynucleotides operably linked to a cellulose synthase promoter.

WO 00/71670 A2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/13637

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/05, 15/09, 15/29, 15/52, 15/82; A01H 5/00

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 800/278, 286, 287, 295, 298; 435/69.1, 320.1, 419; 536/23.2, 23.6, 24.1, 24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN/CAS, WEST 2.0

terms: SEQ ID NO: 1-5, cellulose synthase, UDP-glucose, homologous and heterologous, transgenic plant, antisense.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	WO 98/18949 A1 (CALGENE, INC.) 07 May 1998 (07.05.98), see pages 19-30.	1-4 ----- 9-16, 25-31, 35, 40, 42-43, 45-46
X - Y	WO 98/00549 A (THE AUSTRALIAN NATIONAL UNIVERSITY) 08 January 1998 (08.01.98) see pages 2-11 and 79-81.	1-4 ----- 9-16, 25-31, 35, 42-43, 45-46



Further documents are listed in the continuation of Box C.



See patent family annex.

* "A"	Special categories of cited documents. document defining the general state of the art which is not considered to be of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
E	earlier document published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
L	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
O	document referring to an oral disclosure, use, exhibition or other means	
P	document published prior to the international filing date but later than the priority date claimed	*G* document member of the same patent family

Date of the actual completion of the international search

18 OCTOBER 2000

Date of mailing of the international search report

14 NOV 2000

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/13637

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-4, 9-16, 25-31, 35, 40, 42-43, 45-46

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/13637

A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

800/278, 286, 287, 295, 298; 435/69.1, 320.1, 419; 536/23.2, 23.6, 24.1, 24.5

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-4, 9-16, 25-31, 35, 40, 42-43, 45-46, drawn to polynucleotide having specific nucleic acid sequence or a fragment thereof encoding a functional domain of a cellulose synthase, methods of altering cellulose content of a transgenic plant.

Group II, claim(s) 5-7, 32, 36-39, 41-44, drawn to cellulose synthase promoters and methods of their use.

Group III, claim(s) 8, drawn to cellulose synthase polypeptides

Group IV, claim(s) 17, 19-24, drawn to a polynucleotide encoding UDP-glucose binding domain, and transgenic plants expressing it.

Group V, claim(s) 18, drawn to UDP-glucose polypeptide.

Group VI, claim(s) 33-34, drawn to a method of identifying regulatory elements in a cellulose synthase promoter.

The inventions listed as Groups I-VI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The claimed polynucleotide sequences or a fragment thereof encoding a functional domain of a cellulose synthase is anticipated by Stalker et al (WO 98/18949) who teach plant cDNAs encoding functional units of cellulose synthase, and so do not constitute a single special technical feature which would be an advance over the prior art.

The invention of Group I, drawn to a polynucleotide encoding cellulose synthase, requires a polynucleotide with specific sequence and transgenic plants expressing it, which are not required by any of the other groups.

The invention of Group II, drawn to cellulose synthase promoter and a mechanical stress to a plant which are not required by any of the other groups.

The invention of Group III requires isolated cellulose synthase polypeptides which are not required by any of the other groups.

The invention of Group IV requires polynucleotides encoding UDP-glucose binding domain which are not required by any of the other groups.

The invention of Group V requires UDP-glucose polypeptide which is not required by any of the other groups.

The invention of Group VI requires methods for identifying regulatory elements which are not required by any of the other groups.